

nents that comprise more than one subunit unless specifically stated otherwise. The use of the term “portion” can include part of a moiety or the entire moiety. When a numerical range is mentioned, e.g., 1-5, all intervening values are explicitly included, such as 1, 2, 3, 4, and 5, as well as fractions thereof, such as 1.5, 2.2, 3.4, and 4.1.

**[0257]** “About” or “~” means, when modifying a quantity (e.g., “about” 3 mM), that variation around the modified quantity can occur. These variations can occur by a variety of means, such as typical measuring and handling procedures, inadvertent errors, ingredient purity, and the like.

**[0258]** “Comprising” and “comprises” are intended to mean that the formulations and methods include the listed elements but do not exclude other unlisted elements. The terms “consisting essentially of” and “consists essentially of,” when used in the disclosed methods include the listed elements, exclude unlisted elements that alter the basic nature of the formulation and/or method, but do not exclude other unlisted elements. A formulation consisting essentially of elements would not exclude trace amounts of other elements, such as contaminants from any isolation and purification methods or pharmaceutically acceptable carriers (e.g., phosphate buffered saline), preservatives, and the like, but would exclude, for example, additional unspecified amino acids. The terms “consisting of” and “consists of” when used to define formulations and methods exclude more than trace elements of other ingredients and substantial method steps for administering the compositions described herein. Embodiments defined by each of these transition terms are within the scope of this disclosure.

1. A method of increasing stability of a first antibody or antibody variant, comprising substituting glycine, alanine, or serine at heavy chain position 56 (Aho numbering) to create a second antibody or antibody variant, wherein the second antibody or antibody variant is more stable than the unsubstituted first antibody or antibody variant.

2. The method of claim 1, wherein the glycine is substituted at heavy chain position 56.

3. The method of claim 1, wherein the second antibody or antibody variant is further substituted with a hydrophobic amino acid residue at heavy chain position 80 (Aho numbering), wherein the hydrophobic amino acid residue is selected from the group consisting of: alanine, isoleucine, phenylalanine, leucine, methionine, and valine.

4. (canceled)

5. The method of claim 3, wherein the hydrophobic amino acid residue is selected from the group consisting of: phenylalanine, leucine, and valine.

6. The method of claim 1, wherein the second antibody or antibody variant is further substituted with methionine or isoleucine at position 80 (Aho numbering).

7. (canceled)

8. A method of increasing stability of a first antibody or antibody variant, comprising substituting a hydrophobic amino acid residue at heavy chain position 80 (Aho numbering) of the first antibody or antibody variant to create a second antibody or antibody variant, wherein the second antibody or antibody variant is more stable than the unsubstituted first antibody or antibody variant, wherein the hydrophobic amino acid residue is selected from the group consisting of: alanine, isoleucine, leucine, methionine, phenylalanine, threonine and valine.

9. (canceled)

10. The method of claim 8, wherein the hydrophobic amino acid residue is selected from the group consisting of: phenylalanine, leucine, and valine.

11. (canceled)

12. The method of claim 8, wherein the methionine or isoleucine is substituted at heavy chain position 80 of the first antibody or antibody variant.

13. (canceled)

14. The method of claim 8, wherein the second antibody or antibody variant is further substituted with alanine, glycine, or serine at heavy chain position 56 (Aho numbering).

15. The method of claim 8, wherein the second antibody is further substituted with alanine or glycine at heavy chain position 56 (Aho numbering).

16. The method of claim 8, wherein the second antibody or antibody variant is further substituted with glycine at heavy chain position 56 (Aho numbering).

17-24. (canceled)

25. The method of claim 1, wherein the first antibody or antibody variant is a monoclonal antibody.

26. The method of claim 25, wherein the first antibody is a human monoclonal antibody, humanized monoclonal antibody, or a humanized monoclonal antibody variant.

27. The method of claim 1, wherein the first antibody or antibody variant is an IgG antibody selected from the group consisting of an IgG1, IgG2, IgG3, and IgG4 antibody.

28-54. (canceled)

55. The method of claim 1, wherein the first antibody or antibody variant is a multi-specific antibody.

56. (canceled)

57. The method of claim 1, wherein the first antibody or antibody variant is an antibody fragment that can bind an antigen, wherein the antibody fragment is selected from the group consisting of a Fab fragment, a Fab' fragment, a F'(ab)2 fragment, an Fv fragment, a single chain antibody, diabodies, a biparatopic peptide, a domain antibody (dAb), a CDR-grafted antibody, a single-chain antibody (scFv), a single chain antibody fragment, a chimeric antibody, a diabody, a triabody, a tetrabody, a minibody, a linear antibody; a chelating recombinant antibody, a tribody, a bibody, an intrabody, a nanobody, a small modular immunopharmaceutical (SMIP), an antigen-binding-domain immunoglobulin fusion protein, a single domain antibody, and a VHH containing antibody.

58-93. (canceled)

94. The method of claim 14, wherein the second antibody or second antibody variant is substituted with any one of the following pairs of residues at positions 56 and 80 of the heavy chain (Aho numbering), respectively: GF, GI, GL, GT, GV, AF, AI, AL, AV, AA, AM, SA, SI, or ST.

95. The method of claim 1, further comprising formulating the second antibody or second antibody variant into a pharmaceutical composition.

96. An antibody or antibody variant made by the method of claim 1.

97. A pharmaceutical composition comprising the antibody or antibody variant of claim 96.

98-100. (canceled)

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